



PTO/SB/08a (08-03)  
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Subsection 1.1449/PTO

## INFORMATION DISCLOSURE STATEMENT BY APPLICANT

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Sheet 1 of 3

### Complete if Known

Application Number	10/650,613
Filing Date	August 27, 2003
First Named Inventor	Geenen, Vincent
Art Unit	1647
Examiner Name	
Attorney Docket Number	ULS-001.01

### U.S. PATENT DOCUMENTS

Examiner Initials *	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code <sup>2</sup> (if known)			
286	AA	US-6,197,926 B1	03/06/2001		

### FOREIGN PATENT DOCUMENTS

Examiner Initials *	Cite No. <sup>1</sup>	Foreign Patent Document	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear	T <sup>6</sup>
		Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)				

### NON PATENT LITERATURE DOCUMENTS

Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	AB	Durinov-Bello I. The Role of T Cells, MHC Molecules and Autoantigens. Autoimmunity 27:159-177 (1998)	
	AC	Griffin, A.C. et al. Experimental Autoimmune Insulinitis. Induction by T lymphocytes Specific for a Peptide of Proinsulin. American Journal of Pathology 147:845-857 (1995)	
	AD	Kahn, et al. Genetics of Non-Insulin-Dependent (Type-II) Diabetes Mellitus. Annu. Rev. Med. 47:509-531 (1996)	
	AE	Dev, S.B. et al. Electrochemotherapy - a novel method of cancer treatment. Cancer Treatment Reviews 20:105- 115 (1994)	
	AF	Campos, M. et al. Role of Interferon- $\gamma$ in Inducing Cytotoxicity of Peripheral Blood Mononuclear Leukocytes to Bovine Herpesvirus Type 1 (BHV-1)-Infected Cells. Cellular Immunology 120:259-269 (1989)	
	AG	Allea, D.G. et al. Immunological Characterization and Therapeutic Activity of an Altered-Peptide Ligand, NBI- 6024, Based on the Immunodominant Type 1 Diabetes Autoantigen Insulin B-Chain (9-23) Peptide. Diabetes 51:2126-2134 (2002)	
	AH	Ziegler, A.G. et al. Life-Table Analysis of Progression to Diabetes of Anti-Insulin Autoantibody-Positive Relatives of Individuals With Type 1 Diabetes. Diabetes 38:1320-1325 (1989)	
	AI	Vardi, P. et al. Concentration of Insulin Autoantibodies at Onset of Type 1 Diabetes: Inverse Log-linear Correlation with Age. Diabetes Care 11:736-739 (1988)	

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Date  
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**INFORMATION DISCLOSURE  
STATEMENT BY APPLICANT**

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Sheet 2 of 3

Application Number	10/650,613
Filing Date	August 27, 2003
First Named Inventor	Geenen, Vincent
Art Unit	1647
Examiner Name	
Attorney Docket Number	ULS-001.01

198	AJ	Geenen, V. et al. The Intrathymic Expression of Insulin-related Genes: Implications for Pathophysiology and Prevention of Type 1 Diabetes. <i>Diabetes Metabolism Reviews</i> 14:95-103 (1998)	
	AK	Pozzilli, P. et al. No Effect of Oral Insulin on Residual Beta-Cell Function in Recent-Onset Type 1 Diabetes (the IMDIAB VII). <i>Diabetologia</i> 43:1000-1004 (2000)	
	AL	Dunkley, M.G. et al. Direct Retroviral-Mediated Transfer of a Dystrophin Minigene Into mdx Mouse Muscle in vivo. <i>Human Molecular Genetics</i> 2:717-723 (1993)	
	AM	Delovitch, T.L. et al. The Nonobese Diabetic Mouse as a Model of Autoimmune Diabetes: Immune Dysregulation Gets the NOD. <i>Immunity</i> 7:727-738 (1997)	
	AN	Martens, H. et al. The Thymic Repertoire of Neuroendocrine Self-antigens: Physiological Implications in T-cell life and Death. <i>Immunology Today</i> 12:312-317 (1998)	
	AO	Semple, John W. et al. Processing and Presentation of Insulin. III. Insulin Degrading Enzyme: A Neutral Metalloendoproteinase that is Non-homologous to Classical Endoproteinases Mediates the Processing of Insulin Epitopes for Helper T Cells. <i>International Immunology</i> 4:1161-1167 (1992)	
	AP	Sprent, J. Central Tolerance of T Cells. <i>Intern. Rev. Immunol.</i> 13:5-105 (1995)	
	AQ	Wegmann, D.R. et al. Analysis of the Spontaneous T Cell Response to Insulin in NOD Mice. <i>Journal of Autoimmunity</i> 7, 833-843 (1994)	
	AR	Alleva, D.G. et al. A Disease-associated Cellular Immune Response in Type 1 Diabetics to an Immunodominant Epitope of Insulin. <i>The Journal of Clinical Investigation</i> 107:173-180 (2001)	
	AS	Liu, E. et al. Anti-peptide Autoantibodies and Fatal Anaphylaxis in NOD Mice in Response to Insulin Self-Peptides B:9-23 and B:13-23. <i>The Journal of Clinical Investigation</i> 110:1021-1027 (2002)	
	AT	Bonomo, A. et al. Thymus Epithelium Induces Tissue-Specific Tolerance. <i>The Journal of Experimental Medicine</i> 177:1153-1164 (1993)	
	AU	Czarniecki, C.W. et al. In Vitro Biological Activities of Escherichia Coli-Derived Bovine Interferons- $\alpha$ , - $\beta$ , and - $\gamma$ . <i>Journal of Interferon Research</i> 8:29-37 (1988)	
	AV	Geenen, V. et al. Thymic Expression of Neuroendocrine Self-Peptide Precursors: Role in T Cell Survival and Self-Tolerance. <i>Journal of Neuroendocrinology</i> 10:811-822 (1998)	
	AW	Chailous, L. et al. Oral Insulin Administration and Residual $\beta$ -cell Function in Recent-onset Type 1 Diabetes: a Multicentre Randomised Controlled Trial. <i>The Lancet</i> 356:545-549 (2000)	
	AX	Rudy, G. et al. Similar Peptides from Two $\beta$ Cell Autoantigens, Proinsulin and Glutamic Acid Decarboxylase, Stimulate T Cells of Individuals at Risk for Insulin-Dependent Diabetes. <i>Molecular Medicine</i> 1:625-633 (1995)	
	AY	Kisielow, P. et al. Tolerance in T-cell-receptor Transgenic Mice Involves Deletion of Nonmature CD4 <sup>+</sup> 8 <sup>+</sup> Thymocytes. <i>Nature</i> 333:742-746 (1988)	
	AZ	Ragot, T. et al. Efficient Adenovirus-mediated Transfer of a Human Minidystrophin Gene to Skeletal Muscle of mdx Mice. <i>Nature</i> 361:647-650 (1993)	
	BA	Pugliese, A. et al. The Insulin Gene is Transcribed in the Human Thymus and Transcription Levels Correlate with Allelic Variation at the INS VNTR-IDDM2 susceptibility locus for Type 1 Diabetes. <i>Nature Genetics</i> 15:293-297 (1997)	
	BB	Vafiadis, P. et al. Insulin Expression in Human Thymus is Modulated by INS VNTR alleles at the IDDM2 Locus. <i>Nature Genetics</i> 15:289-292 (1997)	

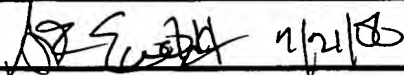
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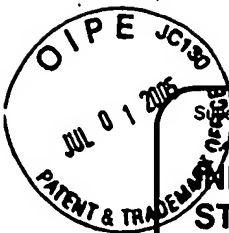
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Date  
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		Filing Date	August 27, 2003
		First Named Inventor	Geenen, Vincent
		Art Unit	1647
		Examiner Name	
Sheet 3 of 3	Attorney Docket Number	ULS-001.01	

BC	Kappos, L. et al. Induction of a Non-encephalitogenic Type 2 T Helper-cell Autoimmune Response in Multiple Sclerosis After Administration of an Altered Peptide Ligand in a Placebo-controlled, Randomized Phase II Trial. <i>Nature Medicine</i> 6:1176-1182 (2000)	
BD	Atkinson, M.A. The Pathogenesis of Insulin-Dependent Diabetes Mellitus. <i>The New England Journal of Medicine</i> 346:1685-1691 (2002)	
BE	DPT-Type 1 Diabetes Study Group Effects of Insulin in Relatives of Patients with Type 1 Diabetes Mellitus. <i>The New England Journal of Medicine</i> 346:1685-1691 (2002)	
BF	Jolicœur, C. et al. T-cell Tolerance Toward a Transgenic $\beta$ -cell Antigen and Transcription of Endogenous Pancreatic Genes in Thymus. <i>Proc. Natl. Acad. Sci. USA</i> 91:6707-6711 (1994)	
BG	Greenen, V. et al. Evidence That Insulin-like Growth Factor 2 (IGF2) is the Dominant Thymic Peptide of the Insulin Superfamily. <i>Thymus</i> 21:115-127 (1993)	

Examiner Signature	 11/21/03	Date Considered	
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			Filing Date	August 27, 2003
			First Named Inventor	Geenen, V.
			Art Unit	1647
			Examiner Name	Saoud, C.
			Attorney Docket Number	ULS-001.01
Sheet	1	of	1	

U.S. PATENT DOCUMENTS					
Examiner Initials *	Cite No. <sup>1</sup>	Document Number	Publication Date MM-DD-YYYY	Name of Patentee or Applicant of Cited Document	Pages, Columns, Lines, Where Relevant Passages or Relevant Figures Appear
		Number - Kind Code <sup>2</sup> (if known)			

FOREIGN PATENT DOCUMENTS						
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		Country Code <sup>3</sup> - Number <sup>4</sup> - Kind Code <sup>5</sup> (if known)				
	BH	EP 0 266 057 A	05-04-1988	Merck & Co.		

NON PATENT LITERATURE DOCUMENTS			
Examiner Initials *	Cite No. <sup>1</sup>	Include name of the author (in CAPITAL LETTERS), title of the article (when appropriate), title of the item (book, magazine, journal, serial, symposium, catalog, etc.), date, page(s), volume-issue number(s), publisher, city and/or country where published.	T <sup>2</sup>
	BI	<del>PCT International Search Report, mailed on February 23, 2004.</del> Author?	
	BJ	Geenen, et al. Role of the Thymus in the Development of Tolerance and Autoimmunity towards the Neuroendocrine System. Ann. N.Y. Acad. Sci. 992:186-195 (2003).	
	BK	Geenen, et al. Thymus tolerance dysfunction in the development of the autoimmune diabetogenic response: a way for a novel type of vaccine/immunotherapy. Diabetologia, 46:A10 (2003).	
	BL	Nakayama, et al. Prime role for an Insulin epitope in the development of type 1 diabetes in NOD mice. Nature 435:220-223 (2005).	
	BM	Kent, et al. Expanded T cells from pancreatic lymph nodes of type 1 diabetic subjects recognize an insulin epitope. Nature 435:224-228 (2005).	
	BN	Skyler, J. Effects of Insulin in Relatives of Patients with Type 1 Diabetes Mellitus. The New England Journal of Medicine, 346, 22:1685-1691b (2002).	
	BO	Johnnidis, et al. Chromosomal clustering of genes controlled by the aire transcription factor. PNAS, 102, 20: 7233-7238 (2005).	
	BP	Geenen, et al. Presentation of Neuroendocrine Self in the Thymus: Toward a Novel Type of Vaccine/Immunotherapy. Drug Design Reviews - Online 1, 37-42 (2004).	
	BQ	Geenen, et al. An Insulin-like Growth Factor 2-Derived Self-Antigen Inducing a Regulatory Cytokine Profile after Presentation to Peripheral Blood Mononuclear Cells from DQ8* Type 1 Diabetic Adolescents. Ann. N.Y. Acad. Sci. 1037:59-64 (2004).	

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